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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/813,191	03/29/2004	Yoshihiko Makino	JG-YY-4979D	5825

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EXAMINER	
MUMMERT, STEPHANIE KANE	
ART UNIT	**PAPER NUMBER**
1637	

DATE MAILED: 03/27/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/813,191	MAKINO ET AL.	
	Examiner	Art Unit	
	Stephanie K. Mummert	1637	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *27 February 2006*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *10-16* is/are pending in the application.

4a) Of the above claim(s) *16* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *10-15* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Election/Restrictions

1. Applicant's election without traverse of Group I, claims 10-15 in the reply filed on February 28, 2006 is acknowledged.

Claim 16 is withdrawn from further consideration pursuant to 37 CFR 1.142(b) as being drawn to a nonelected invention, there being no allowable generic or linking claim. Election was made **without** traverse in the reply filed on February 28, 2006.

Claims 10-15 are pending and will be examined.

Claim Rejections - 35 USC § 112

2. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

3. Claims 10 and 12 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Regarding claim 10, the use of the term "having a hydrophilic moiety at each one end" is confusing. It cannot be determined if each end of the spacer has a hydrophilic moiety or each spacer has a hydrophilic moiety at one end.

Regarding claim 12, the meaning of the term "mol./mm2" is unclear. Is the term "mol." Intended to represent molecules or moles?

4. Claim 12 recites the limitation "the DNA fragments" in the body of the claim. There is insufficient antecedent basis for this limitation in the claim.

Claim Rejections - 35 USC § 102

(a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

(e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

5. Claims 10-14 are rejected under 35 U.S.C. 102(e) as being anticipated by Tarlov et al. (US Patent 5,942,397; August 1997). Tarlov teaches a biopolymer containing monolayer comprising: thiol-derivatized biopolymers and organic thiols bound to a metal substrate (Abstract).

With regard to claim 10, Tarlov teaches a PNA chip comprising a solid carrier and a plurality of PNA fragments fixed onto the solid carrier at each one end, wherein a plurality of short chain spacer molecules having a hydrophilic moiety at each one end are fixed at each another end onto a surface area of the solid carrier having no PNA fragments thereon (Figure 4B, where spacers separate single stranded DNA molecules on a gold substrate; col. 2, where oligonucleotide refers to DNA, RNA and PNA; col. 3, lines 26-59).

With regard to claim 11, Tarlov teaches an embodiment of claim 10, wherein the solid carrier is an electro-conductive substrate (col. 3, lines 20-25, where the preferred substrate is a metal substrate, including gold, silver, copper and platinum).

With regard to claim 12, Tarlov teaches an embodiment of claim 10, wherein the DNA fragments are fixed onto the solid carrier in an amount of 10^{-20} to 10^{-12} mo./mm2 (Figure 6).

With regard to claim 13, Tarlov teaches an embodiment of claim 10, wherein the hydrophilic moiety of the spacer molecule is a hydroxyl group (col. 3, lines 29-37, where hydroxy terminated organic thiols are preferred; see also Figure 4B).

With regard to claim 14, Tarlov teaches an embodiment of claim 10, wherein the spacer molecule is fixed onto the solid carrier through a mercapto moiety attached to the end of the spacer molecule (col. 3, lines 29-37, where hydroxy terminated organic thiols such as mercaptohexanol are preferred; see also Figure 4B).

Claim Rejections - 35 USC § 103

6. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

7. Claims 10-11 and 13 rejected under 35 U.S.C. 103(a) as being unpatentable over Bamdad et al. (US Patent 6,197,515; March 2001) in view of Egholm et al. (Nature, 1993, vol. 365, p. 566-568). Bamdad teaches a biosensor to which is attached a self-assembled monolayer (Abstract).

With regard to claim 10, Bamdad teaches a DNA or RNA chip comprising a solid carrier and a plurality of DNA or RNA fragments fixed onto the solid carrier at each one end, wherein a plurality of short chain spacer molecules having a hydrophilic moiety at each one end are fixed at

each another end onto a surface area of the solid carrier having no PNA fragments thereon (Figures 8-9, col. 15, line 61 to col. 16, line 40, where a self-assembled monolayer is provided which includes a major component species 30 and a minor component 32 which is an SAM-forming species including a nucleic acid strand and where these nucleic acid strands are isolated from other nucleic acid strands and is surrounded by the major component species; see also col. 10, line 62 to col. 11 line 13, where the 'major' species' has a formula X-R-NSBi, where NSBi is a non-specific-binding inhibitor and can be selected from such groups as –CH3 and –OH, and where X is a functional group that adheres to the surface and R represents a spacer moiety).

With regard to claim 11, Bamdad teaches an embodiment of claim 10, wherein the solid carrier is an electro-conductive substrate (col. 11, lines 14-40, where multiple substrates are contemplated including metals, silica, quartz, glass and epoxy compounds).

With regard to claim 13, Bamdad teaches an embodiment of claim 10, wherein the hydrophilic moiety of the spacer molecule is a hydroxyl group (col. 10, line 62 to col. 11 line 13, where the 'major' species' has a formula X-R-NSBi, where NSBi is a non-specific-binding inhibitor and can be selected from such groups as –CH3 and –OH, and where X is a functional group that adheres to the surface and R represents a spacer moiety).

Regarding claim 10, Bamdad does not specifically teach the inclusion of PNA or peptide nucleic acids into the biosensor chip, however Bamdad specifically teaches the inclusion of DNA or RNA nucleic acids (col. 7, lines 41-44). Egholm teaches the formation of a DNA analogue, PNA, which is capable of hybridizing to complementary oligonucleotides obeying the Watson-Crick basepairing rules and is a DNA mimic (Abstract).

It would have been prima facie obvious to one of ordinary skill in the art at the time the invention was made to have substituted PNA for DNA in the biosensor disclosed by Bamdad with a reasonable expectation for success. As noted by Egholm, "The PNA backbone is uncharged and we ascribe the increased thermal stability of the PNA-DNA duplex relative to that of the DNA-DNA duplex predominantly to lack of electrostatic repulsion between the two strands" (p. 567, col. 2, top paragraph). Egholm also notes "Note that for virtually all base-pair mismatches, the decrease in thermal stability is greater for the PNA-DNA complex than for the DNA-DNA complex, suggesting (provided that the differences in transition enthalpies are identical) that the sequence discrimintation is, if anything, more efficient for PNA recognizing DNA than for DNA recognizing DNA" (p. 566, col. 2, middle paragraph). Therefore, due to the efficient sequence-specific recognition of DNA by PNA, one of ordinary skill in the art at the time the invention was made would have been motivated to include PNA in addition to DNA and RNA into the biosensor disclosed by Bamdad with a reasonable expectation for success.

7. Claim 15 is rejected under 35 U.S.C. 103(a) as being unpatentable over Tarlov as applied to claims 10-14 above, and further in view of Takenaka et al. (Analytical Chemistry, 2000, vol. 72, p. 1334-1341). Tarlov teaches a biopolymer containing monolayer comprising: thiol-derivatized biopolymers and organic thiols bound to a metal substrate (Abstract).

Tarlov teaches the limitations of claims 10-14 as recited in the 102 rejection stated above. However, regarding claim 15, Tarlov does not teach the use of spacers comprising 2-mercaptoethanol.

With regard to claim 15, Takenaka teaches an embodiment of claim 10, wherein the spacer molecule is derived from a compound selected from the group consisting of 2-mercaptoethanol (p. 1336, col. 1, 'immobilization of DNA on a gold electrode' heading, where electrodes of reduced DNA modification density were prepared analogously by coadsorption of -2-mercaptoethanol).

It would have been prima facie obvious to one of ordinary skill in the art at the time the invention was made to apply the 2-mercaptoethanol spacer molecules taught by Takenaka to the monolayer taught by Tarlov with a reasonable expectation for success. As noted by Takenaka, "it should be noted that the treatment with 2-ME was essential in order to obtain reproducible responses for all these measurements on thinly modified dA20 electrodes. The thiol strongly adsorbs on the gold surface, and it was presumed that 2-ME eliminated an undesired secondary interaction of the probe strand with the bare portion of the metal surface by making it chemically inert" (p. 1340, col. 1, top paragraph). Therefore, because Takenaka and Tarlov are directed to similar goals with regards to avoiding non-specific binding where no oligonuclotide is bound, and given the stated benefit that the inclusion of 2-ME allowed for reproducible measurements, one of ordinary skill in the art at the time the invention was made would have been motivated to apply the 2-mercaptoethanol spacer molecules taught by Takenaka to the surface taught by Tarlov with a reasonable expectation for success.

Conclusion

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Stephanie K. Mummert whose telephone number is 571-272-8503. The examiner can normally be reached on M-F, 8:30-5.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Gary Benzion can be reached on 571-272-0782. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Stephanie K. Mummert

Stephanie K Mummert
Examiner
Art Unit 1637

SKM

Kenneth R. Horlick

KENNETH R. HORLICK, PH.D
PRIMARY EXAMINER

3/20/06